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10/578,521	05/08/2006	Jong-Yoon Chun	50413/015001	7873

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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/578,521	CHUN, JONG-YOON	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *8,12 and 23-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11,13-22 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I invention claims 1-25 and 30 in the reply filed on June 19, 2008 is acknowledged. Applicant has also elected species (i) primer of formula I. Non elected claims withdrawn from consideration are 8, 12, 23-29. Claims that read upon elected species from the elected group are 1-7, 9-11, 13-22 and 30. Consequently claims 1-7, 9-11 and 13-22 and 30 will be examined in this action.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on May 8, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Interpretation

3. The claims currently under consideration are method claims for amplifying nucleic acids. The claims recite structural limitations of the primers used in the method. No specific template nucleic acid is recited in the claims. In view of this scenario, the limitations wherein specific portions of said primers are substantially complementary to, a template nucleic acid, therefore reads on a method where the claims encompass primers for any conceivable nucleic acid template, whether naturally occurring or man-made, whether known to exist or capable of being synthesized. Any conceivable nucleic acid sequence can be synthesized and engineered in such a way as to produce gDNA, cDNA or mRNA. In this regard, those particular limitations of the claims pertaining to substantial complementarity are met by any primer depending on the

template nucleic acid. Since no specific template is recited in the claims, limitations based on hybridization to random or arbitrary sequence with respect to an unspecified template impart no structural limitation on the claimed primers that are useful in the method, therefore any primer will function in the claimed method.

Although the references upon which the 35 U.S.C. 102 rejections below are based may disclose a "template" or "target" for the primers taught, such templates or targets are not limiting in the application of the disclosed primers as prior art against the claims because the prior art primers could be used with other targets or templates.

DNA Walking annealing control primer (DW-ACP) has not been defined, so using broadest reasonable interpretation any primer used in prior art will read upon claim 1 as currently recited.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-5, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stone & Wharton (1994) Nucleic acids Research vol. 22, no 13 pages 2612 -2618 as evidenced by Welsh & McClelland (1990) Nucleic acids Research vol. 18, no 24 pages 7213-7218 in view of Brenner (US pat. 5,962,228 issued Oct 5, 1999).

Regarding claim 1, Stone & Wharton teach a method for amplifying an unknown nucleotide sequence adjacent to a known nucleotide sequence, which comprises the step of

(a) performing a primary amplification of said unknown nucleotide sequence using a DNA walking annealing control primer (DW-ACP) (see abstract where amplification of cDNA using an arbitrary primer is taught. Arbitrary primer of Stone & Wharton = DNA walking annealing control primer (DW-ACP) of instant claim)

and a first target-specific primer (see abstract of Stone & Wharton where the primer that is member of primer set which corresponds to a conserved region within a specific gene family = the first target specific primer of instant claims); in which said step (a) comprises:

(a-I) performing a first-stage amplification of said unknown nucleotide sequence at a first annealing temperature, comprising at least one cycle of primer annealing, primer extending and denaturing using a first degenerate DW-ACP containing a degenerate random nucleotide sequence to hybridize with said unknown nucleotide sequence and a hybridizing nucleotide sequence substantially complementary to a site on said unknown nucleotide sequence, wherein said first annealing temperature enables said first degenerate DW-ACP to function as a primer, whereby a first degenerate DW-ACP extension product is generated (see last line of page 2612 and beginning of par. 1 on page 2613 where amplification is conducted using both the arbitrary primer as well as primer specific for a conserved region of gene family is

taught. The annealing temperature of first cycle is taught as temperature between 40^0C to 50^0C; and

(a-2) performing a second-stage amplification at a second annealing temperature (see page 2613 where second-stage amplification at a second annealing temperature of 50^0C to 60^0C is taught).

Stone & Wharton do not state that at this second annealing temperature the first degenerate DW-ACP ceases to function as a primer. Stone & Wharton have developed the method based on modification of protocol published by Welsh and McClelland (see abstract). Welsh and McClelland in their 1990 paper (Nucleic acids Research vol. 18, no 24 pages 7213-7218) where they first described arbitrary primed PCR teach the rationale why at higher annealing temperature said first degenerate DW-ACP ceases to function as a primer. They teach cycling at lower temperature for two cycles (annealing at 40^0C)—low stringency annealing followed by amplification under high stringency cycles (annealing at 60^0C) (see page 7214 par. 1). They state "at a sufficiently low temperature, primers (Arbitrary primer PCR primers---note added by Examiner) can be expected to anneal to many sequences with a variety of mismatches". (see results section par. 2 on page 7214). On page 7215 where they determine the effect of temperature on Arbitrary primed PCR they state "The pattern of bands changes slightly as the temperature is raised, until, at some point, the temperature is too high for this set of matches to predominate". The bands were being formed due to annealing of the arbitrary primers to the template and subsequent extensions. In view of this explicit teaching of Welsh and McClelland it is clear that as temperature is increased at some

temperature the arbitrary primer ceases to anneal in other words it ceases to function as a primer. Thus Stone & Wharton as evidenced by Welsh and McClelland teach

(a-2) performing a second-stage amplification at a second annealing temperature to render said first degenerate DW-ACP not to function as a primer, comprising:

(a-2-1) amplifying said first degenerate DW-ACP extension product using said first target-specific primer to hybridize with a target-specific nucleotide sequence substantially complementary to a site on said known nucleotide sequence, whereby a target-specific primer extension product is generated (in the amplification mix only the arbitrary primer=DW-ACP and first target specific primer and the first degenerate DW-ACP extension product produced at end of first stage amplification is present. At the second high stringency annealing temperature range of 50-60^{0}C taught by Stone & Wharton, the arbitrary primer=DW-ACP ceases to function as primer now only the first target specific primer anneals to said first degenerate DW-ACP extension product using said first target-specific primer to hybridize with a target-specific nucleotide sequence substantially complementary to a site on said known nucleotide sequence, whereby a target-specific primer extension product is generated),

Regarding claim 1, Stone & Wharton as evidenced by Welsh and McClelland do not teach:

(a-2-2) amplifying said target-specific primer extension product using a second DW-ACP to hybridize with a nucleotide sequence complementary to said first

degenerate DW-ACP sequence of said target-specific primer extension product, whereby a second DW-ACP extension product is generated, and

(a-2-3) amplifying said second DW-ACP extension product using said second DW-ACP and said first target-specific primer, whereby a primary amplification product without a degenerate random nucleotide sequence is generated.

Regarding claim 1, Brenner (see whole section on rolling primers col 7-col. 11) teaches

(a-2-2) amplifying said target-specific primer extension product using a second DW-ACP (Brenner teaches use of complexity reducing nucleotides in the primers for use in primer walking approach) see col. 7 lines 1-4. Thus by teaching use primer set containing complexity reducing nucleotides Brenner teaches a second DW-ACP) to hybridize with a nucleotide sequence complementary to said first degenerate DW-ACP sequence of said target-specific primer extension product, whereby a second DW-ACP extension product is generated (see col. 7 section rolling primers. Col. 8 lines 45-53 where sequences of the DW-ACPs called rolling primers is shown), and

(a-2-3) amplifying said second DW-ACP extension product using said second DW-ACP and said first target-specific primer, whereby a primary amplification product without a degenerate random nucleotide sequence is generated. (see col. 9 lines 9-58 where the process is taught how using primers P1 and P2 a primary amplification product without a degenerate random nucleotide sequence is generated).

Regarding claim 2, Welsh and McClelland teaches wherein said first-stage amplification is performed for one cycle (see page 7214 par. 1 where two cycle of

primer annealing, primer extending and denaturing are taught. Thus teaching wherein said first-stage amplification is performed for one cycle).

Regarding claim 3, Welsh and McClelland teaches wherein said second-stage amplification is performed for at least 5 cycles (see page 7214 par. 1 where 10 cycles of high stringency second-stage amplification is taught. Thus teaching wherein said second-stage amplification is performed for at least 5 cycles).

Regarding claim 4, Stone and Wharton teaches wherein said first annealing temperature is between about 35°C and 50°C (see page 2613 par. 1 where range of first annealing temperature from about 40°C to 50°C is taught. Thus Stone and Wharton teaches said first annealing temperature is between about 35°C and 50°C).

Regarding claim 5, Stone and Wharton teaches wherein said second annealing temperature is between about 50°C and 72°C (see page 2613 par. 1 where annealing temperature is between 50°C to 60°C is taught. Thus Stone and Wharton teach wherein said second annealing temperature is between about 50°C and 72°C).

Regarding claim 13, Stone & Wharton teaches wherein said nucleotide sequence to be amplified is gDNA or cDNA (see page 17 line 1 where nucleotide sequence to be amplified is taught to be gDNA or cDNA).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Brenner in the method of Stone & Wharton as evidenced by Welsh and McClelland. The motivation to do so is provided to one of ordinary skill in the art by teachings of Brenner.

Stone & Wharton as evidenced by Welsh and McClelland teach a method for amplifying an unknown nucleotide sequence adjacent to a known nucleotide sequence. These amplified fragments were run on gel to identify how many different regions were amplified, then the DNA was extracted from gel slices before it was reamplified, cloned into plasmids before the sequencing could be performed to identify DNA sequence of the unknown nucleotide sequence (see page 2613 par. 2-4 of methods section).

Brenner teaches a method of using rolling primers (see col. 9- col. 12, the entire section dealing with sequencing) where the amplified products can be directly sequenced without requiring the separation of the amplified products on gels their re extraction from gel slices, re amplification and cloning into plasmids. Thus one of ordinary skill in the art realizes the advantages provided by practicing the method of Brenner in the method of Stone & Wharton as evidenced by Welsh and McClelland in terms of ease of performance, arriving at a method that requires less manipulation and is thus also more efficient.

Thus the method Stone & Wharton as evidenced by Welsh and McClelland amplifies an unknown nucleotide sequence adjacent to a known nucleotide sequence and the method of Brenner allows unambiguous identification of the DNA sequence of this unknown nucleotide sequence because in the method of Brenner "the primers "roll" along the polynucleotide during the sequencing process, moving a base at a time along the template with each cycle" (see last part of abstract).

6. Claims 6-7, 9-11, and 14-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stone & Wharton as evidenced by Welsh & McClelland; and Brenner

as applied to claim 1 above, and further in view of Liu and Whittier (1995) Genomics 25, 674-681; Watanabe et al. 2001 Journal of Microbiological methods 44 : pp 253-262 and Oberste et al. J Clin. Microbiol. Vol. 37 no 5 May 1999 pp. 1288-1293.

Regarding claim 6, Stone & Wharton as evidenced by Welsh & McClelland; and Brenner teaches the method according to claim 1 and also teach use of arbitrary degenerate primers. But they do not explicitly recite use of a primer where first degenerate DW-ACP has a general formula I:

5'- Xp-Yq-Zr-Qs-3' (I)

Regarding claim 6, Liu and Whittier teach use of an arbitrary degenerate primer (AD) which meets the limitations enunciated for DW-ACP of a general formula I: See primers AD3 and AD4 on page 675.

AD3 primer is 5' CA(A/T)CGICNGAIA(G/C)GAA-3'

5'- Xp-Yq-Zr-Qs-3' (I)

wherein, Xp represents a 5'-end portion having a pre-selected nucleotide sequence (the nucleotides CA at 5' end of AD3 = Xp a 5'-end portion having a pre-selected nucleotide sequence),

Yq represents a regulator portion comprising at least two universal base or non-discriminatory base analog residues (the middle part of primer containing Inosine is regulator portion. Inosine is universal base or non-discriminatory base analog residues. Both primers AD3 and AD4 contain 2 inosine residues. Thus meeting the requirement of the claimed primer),

Zr represents a degenerate random sequence portion having a degenerated random nucleotide sequence (portion of primer having N in it serves as the region containing a degenerate random sequence portion having a degenerated random nucleotide sequence),

Qs represents a 3'-end portion having a hybridizing nucleotide sequence substantially complementary to a site on said unknown nucleotide sequence to hybridize therewith (the 3' end of primer GAA3' serves as Qs represents a 3'-end portion having a hybridizing nucleotide sequence substantially complementary to a site on said unknown nucleotide sequence to hybridize therewith),

p, q, r and s represent the number of nucleotides, and

X, Y, Z and Q are deoxyribonucleotide in this instance.

Regarding claim 7, Liu and Whittier teaches wherein said regulator portion in said first degenerate DW-ACP is capable of restricting the annealing portion of said primer to its 3'-end portion at said first annealing temperature (Examiner would like to point out that no template is specified in the claim and the tm of primer AD3 and AD4 calculated is 47-48^{0}C see materials and methods page 675 section Oligo primers. Therefore this primer containing regulator portion will be inherently capable of annealing portion of said primer to its 3'-end portion at said first annealing temperature other wise no amplification will ensue. In principle an inosine containing regulator portion taught by Liu and Whittier in said first degenerate DW-ACP is capable of restricting the annealing portion of said primer to its 3'-end portion at said first annealing temperature).

Regarding claim 9, Liu and Whittier teaches wherein said method further comprises the step of (c) performing a secondary amplification at a third annealing temperature, comprising a nested target-specific primer designed to amplify an internal region of said primary amplification product. (see page 676 fig. 1 where internal primers SP2 and SP3 are taught for nested PCR referred to as secondary and tertiary PCR in bottom of fig. 1. Thus teaching a nested target-specific primer designed to amplify an internal region of said primary amplification product).

Regarding claim 10, Liu and Whittier teaches annealing temperature is between about 50°C and 72°C (see page 680 par. 2 where guidelines are provided as to how to set annealing temperatures for high stringency conditions. They teach tm's of the specific primers should be at least 10^0C higher than the average tm's of the AD primers, and the annealing temperatures in the high–stringency cycles should be set as high as possible (usually 1-5^0C higher than the calculated specific primers). In the instant case the tm of the AD3 and AD4 primers is 47-48^0C see page 675 par. 3 . So using the guidelines the tm of the specific primers SP2 and SP3 used for nested PCR in this case has to be 57-58^0C. So the third temperature condition for performing high stringency annealing temperature for nested PCR should be at least 1-5^0C higher than the calculated specific primers tm which will be 58-63^0C. Thus by teaching annealing temperature of 58-63^0C, Liu and Whittier teaches annealing temperature is between about 50°C and 72°C).

Regarding claim 11, Liu and Whittier teaches performing nested PCR where a small aliquot of the amplified product is diluted and used as a template for nested PCR

(see page 675 last part of par. 2 in per procedure where secondary and tertiary (nested PCR) PCRs are taught. It would have been prima facie obvious to one of ordinary skill in the art wherein said method further comprises the step (b) of purifying a reaction resultant of the step (a) to remove said first degenerate DW-ACP, said second DW-ACP and said first target-specific primer prior to performing the step (c). One of ordinary skill in the art performs nested PCR to quantify or for un ambiguous detection of the amplified region. Hence the purpose of performing the nested PCR in step C is to obtain specific amplified product with a reasonable yield for further use. During classic nested PCR simply a dilution of the amplified product is done and to this diluted sample, PCR primers needed for nested PCR are added. That means the mixture on which nested PCR is being performed may still contains some of the original template and degenerate primer/first specific target primers. Therefore by performing the purification of the amplified product all primers used in the previous amplification are removed. Thus this purified product can be used as a template for nested PCR with no possibility of interference from the previously used PCR primers. Purification of PCR product prior to performing nested PCR will ensure that only the PCR product that was amplified initially using degenerate primer and target specific primer is amplified further. There will be no carry over of the primers used initially that can generate spurious background or amplification of some other regions primed by annealing of the degenerate primers on the original template that will still be present if only a dilution was performed as is routine in nested PCRs.

Regarding claims 14-16, Liu and Whittier teaches wherein said universal base or non-discriminatory base analog residue is deoxyinosine (see page 675 section oligo primers where inosine containing AD3 and AD4 primers are taught).

Regarding claims 17, Brenner teaches primers wherein contiguous nucleotides having universal base or non-discriminatory base analog residue (see col. 27 line 42 where primer is taught wherein contiguous nucleotides having deoxyinosine (I) are used as universal base or non-discriminatory base analog residue. The purpose of having this stretch is to balance the annealing and melting temperature of the primers (see col. 27 lines 43-45) . The location of the inosines is at the 5' end of primer in case of Brenner and is not in the middle the portion referred to as regulator portion in the instant claim.

It would have been prima facie obvious to one of ordinary skill in the art to use degenerate primers containing a stretch of inosine in the method of Stone & Wharton as evidenced by Welsh & McClelland; and Brenner at the time the invention was made. This is because Brenner taught the use of a stretch of inosines to achieve a desired annealing temperature. If the intent was to change the annealing characteristic of the molecule namely DW-primer then presence of inosine will do it. If the intent was to design a primer which at lower first annealing temperature will anneal to the target using the middle portion as well as the 3' end, and at higher second annealing temperature the portion containing stretch of inosines reduces the tm of the primer as compared to primer with no inosines and this will result in the inosine containing primer not to anneal at higher second annealing temperature. Thus at higher annealing temperature the

inosine containing degenerate primer will cease to act as primer. One of ordinary skill can place the inosines at any desired location in the primer to achieve the desired end.

This is consistent with the Federal Circuit decision in In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003) "We have also held that a prima facie case of obviousness exists when the claimed range and the prior art range do not overlap but are close enough such that one skilled in the art would have expected them to have the same properties." Thus, an ordinary practitioner would have recognized that the location of the stretch of inosines could be adjusted to maximize the desired results. As noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the location of the contiguous stretch of inosines in the middle regulator region was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. As noted, a skilled artisan would expect tm of the resulting primer containing a contiguous stretch if inosines to be lower as compared to the primer containing no inosines , thus reducing the upper limit of the temperature threshold at which this primer can anneal. Thus, an ordinary practitioner would have recognized that the results could be adjusted to maximize the desired results.

Regarding claims 18, Stone and Walker teaches wherein p represents an integer of 10 to 60 (see list of arbitrary primers in table 1C on page 2613. The 5' end of the

primer CE NheI shows p represents an integer of 12 thus teaching wherein p represents an integer of 10 to 60).

Regarding claims 19 and 20, Brenner teaches wherein q is at least 3 (claim 19) or wherein q represents an integer of 2 to 10 (see col. 27 line 42 where primer with 8 Inosines which are universal or no-discriminatory bases is taught. Thus Chun teaches wherein q is at least 3—claim 19 or an integer of 2 to 10 –claim 20).

Regarding claims 21, Liu and Whittier teaches wherein r represents an integer of 2 to 5 (see page 675 sequence of primers AD3 or AD4 where two nucleotide sequences following Inosine represent r. Thus teaching wherein r represents an integer of 2 to 5).

Regarding claims 22, Liu and Whittier teaches wherein s represents an integer of 3 to 10 (see page 675 sequence of primers AD3 or AD4 where last 3 nucleotides at 3' end will be s. Thus Chun teaches s represents an integer of 3 to 10).

It would have been prima facie obvious to one of ordinary skill in the art to practice the method of Liu and Whittier in the method of Stone & Wharton as evidenced by Welsh & McClelland; and Brenner at the time the invention was made. The motivation to do so is provided by both Watanabe et al. and Oberste et al.

Stone & Wharton as evidenced by Welsh & McClelland; and Brenner teach a method for amplifying an unknown nucleotide sequence adjacent to a known nucleotide sequence. The method is also referred to as genome fingerprinting in the art. The arbitrary primers used by Stone & Wharton as evidenced by Welsh & McClelland; and Brenner do not contain universal or non-discriminatory base analogs in the regulator portion of the primers. Liu and Whittier teach two arbitrary primers that contain universal

or non-discriminatory in the regulator portion of the arbitrary primers. These primers also have the right melting temperatures that would meet the annealing temperature range requirements of the instant method. Motivation to use the inosine containing arbitrary primers of Liu and Whittier in the method of Stone & Wharton as evidenced by Welsh & McClelland; and Brenner is provided to one of ordinary skill in the art at the time the invention was made by state of the art at that time. A survey of the literature published in the fingerprinting field tells one of ordinary skill that artisans practicing in the field of fingerprinting have successfully introduced inosines in the universal primers used for amplifying 16S ribosomal DNA from a community of bacteria. These inosine containing degenerate primers were able to reduce amplification biases caused by mismatches that were observed using unmodified universal primers. (see abstract Watanabe et al. 2001). Oberste et al. 1999 designed primers to amplify unknown Enteroviruses (EVs). These primers were designed with inosines to account for the differences between different virus groups and for codon degeneracy (the inosine containing primers are shown in Table 1 page 1289 of Oberste et al. 1999). Using this set of inosine containing degenerate primers they were able to amplify 51 EV strains isolated from clinical material between 1991 and 1998. Art taught that there is high degree of genetic diversity among the EVs and therefore posed a challenge in the systematic design of nucleic acid based diagnostic reagents (see page 1292 par. 2 of discussion). Oberste et al. go on to state "Degenerate inosine containing PCR primers were developed to overcome such nucleotide sequence diversity by specifically targeting regions of conserved amino acid sequences". (see page 1292 last part of par.

2 under discussion). Therefore inosine containing primers have been used by one of ordinary skill in the art for performing fingerprinting.

These teachings of Watanabe et al.; and Oberste et al. teach one of ordinary skill that by using the degenerate primers containing inosines taught by Liu and Whittier in the method of Stone & Wharton as evidenced by Welsh & McClelland; and Brenner they have a reasonable expectation of success in not only being able to successfully perform fingerprinting analysis from diverse unknown bacterial or viral clinical isolates but also accurately determine the nucleic acid sequence of the identified organism.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 30 provides for the use of the method of claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 30 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Conclusion

9. Claims 1-7, 9-11, 13-22 and 30 under consideration are rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

/Teresa E Strzelecka/

Primary Examiner, Art Unit 1637

September 26, 2008